

## Claims

- i. a microemulsion comprising a lipid core and an amphipathic lipid layer

surrounding said lipid core, wherein a hydrophobic portion of said amphipathic lipid layer is associated with said lipid core and a hydrophilic portion of said amphipathic lipid layer is associated with a hydrophilic surface of said amphipathic lipid;

- ii. a bioactive agent; and

- iii. optionally, a lipidized polymer;

said bioactive agent being included in said composition in an effective amount, said amphipathic lipid being included in said composition in an amount effective to form a microemulsion with said lipid core, and said lipidized polymer being included in said composition in association with said amphipathic lipid in an amount ranging from about 0.01% to about 65% by weight of said composition.

2. The composition according to claim 1 wherein said amphipathic lipid includes an amount of a steroid component effective to increase the stability of said amphipathic lipid.

3. The composition according to claim 1 wherein said amphipathic lipid is a phospholipid, including a chemically modified, conjugated or polymerized phospholipid such as pegylated phospholipid.

4. The composition according to claim 1 wherein said phospholipid is selected from the group consisting of phosphatidylcholine, cephalin, isolecithin, phosphatidylethanolamine, distearoylphosphatidylcholine, phosphatidylserine, phosphatidylglycerol, phosphatidic acid, phosphatidylinositol, sphingomyelin, dimyristoylphosphatidylcholine, dimyristoylphosphatidylglycerol, pegylated phospholipids and mixtures, thereof.

5. The composition according to claim 4 wherein said amphipathic lipid layer further comprises about 0.05% to about 25% by weight of a steroidal component.

6. The composition according to claim 5 wherein said steroidal component is selected from the group consisting of cholesterol, pegylated cholesterol, coprostanol, cholestanol,

Study		Population		Intervention		Comparison		Outcome	
Author	Year	N	Age (yr)	Group	Duration (yr)	Group	Duration (yr)	Measure	Value
1	1998	100	65-74	Exercise	1	Control	1	Relative risk	0.75
2	1999	100	65-74	Exercise	1	Control	1	Relative risk	0.75
3	2000	100	65-74	Exercise	1	Control	1	Relative risk	0.75
4	2001	100	65-74	Exercise	1	Control	1	Relative risk	0.75
5	2002	100	65-74	Exercise	1	Control	1	Relative risk	0.75
6	2003	100	65-74	Exercise	1	Control	1	Relative risk	0.75
7	2004	100	65-74	Exercise	1	Control	1	Relative risk	0.75
8	2005	100	65-74	Exercise	1	Control	1	Relative risk	0.75
9	2006	100	65-74	Exercise	1	Control	1	Relative risk	0.75
10	2007	100	65-74	Exercise	1	Control	1	Relative risk	0.75
11	2008	100	65-74	Exercise	1	Control	1	Relative risk	0.75
12	2009	100	65-74	Exercise	1	Control	1	Relative risk	0.75
13	2010	100	65-74	Exercise	1	Control	1	Relative risk	0.75
14	2011	100	65-74	Exercise	1	Control	1	Relative risk	0.75
15	2012	100	65-74	Exercise	1	Control	1	Relative risk	0.75
16	2013	100	65-74	Exercise	1	Control	1	Relative risk	0.75
17	2014	100	65-74	Exercise	1	Control	1	Relative risk	0.75
18	2015	100	65-74	Exercise	1	Control	1	Relative risk	0.75
19	2016	100	65-74	Exercise	1	Control	1	Relative risk	0.75
20	2017	100	65-74	Exercise	1	Control	1	Relative risk	0.75
21	2018	100	65-74	Exercise	1	Control	1	Relative risk	0.75
22	2019	100	65-74	Exercise	1	Control	1	Relative risk	0.75
23	2020	100	65-74	Exercise	1	Control	1	Relative risk	0.75
24	2021	100	65-74	Exercise	1	Control	1	Relative risk	0.75
25	2022	100	65-74	Exercise	1	Control	1	Relative risk	0.75
26	2023	100	65-74	Exercise	1	Control	1	Relative risk	0.75
27	2024	100	65-74	Exercise	1	Control	1	Relative risk	0.75
28	2025	100	65-74	Exercise	1	Control	1	Relative risk	0.75
29	2026	100	65-74	Exercise	1	Control	1	Relative risk	0.75
30	2027	100	65-74	Exercise	1	Control	1	Relative risk	0.75
31	2028	100	65-74	Exercise	1	Control	1	Relative risk	0.75
32	2029	100	65-74	Exercise	1	Control	1	Relative risk	0.75
33	2030	100	65-74	Exercise	1	Control	1	Relative risk	0.75
34	2031	100	65-74	Exercise	1	Control	1	Relative risk	0.75
35	2032	100	65-74	Exercise	1	Control	1	Relative risk	0.75
36	2033	100	65-74	Exercise	1	Control	1	Relative risk	0.75
37	2034	100	65-74	Exercise	1	Control	1	Relative risk	0.75
38	2035	100	65-74	Exercise	1	Control	1	Relative risk	0.75
39	2036	100	65-74	Exercise	1	Control	1	Relative risk	0.75
40	2037	100	65-74	Exercise	1	Control	1	Relative risk	0.75
41	2038	100	65-74	Exercise	1	Control	1	Relative risk	0.75
42	2039	100	65-74	Exercise	1	Control	1	Relative risk	0.75
43	2040	100	65-74	Exercise	1	Control	1	Relative risk	0.75
44	2041	100	65-7						

cholestane, C<sub>1</sub> to C<sub>24</sub> steroidal esters and mixtures, thereof.

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7. The composition according to claim 1 wherein said bioactive agent is selected from the group consisting of anesthetics, systemic antibiotics, antiparasitics, systemic quinolones, anti-infectives, anti-inflammatories, aminoglycosides, cephalosporins, penicillins, antidotes, anti-cholinesterases, metal poisoning antidotes, antineoplastics, 5'-fluorouracil, cytotoxic agents, hormones, steroids, immunomodulators, cytokines, systemic antivirals, systemic antifungals, biologicals, alpha-antitrypsin, bone metabolism regulators, hypercalcemic agent, cardiovascular agents, beta blockers, cerebral vasodilators, cerebral metabolic enhancers, cholinesterase inhibitors, colony stimulating factors, granulocyte-colony stimulating factors, granulocyte macrophage-colony stimulating factors, vasopressors, local diabetic agents, diagnostics such as CT scan enhancers and angiocardiology agents, adenosine deaminase deficiency agents, gonadotropin inhibitors, adrenal cortical steroid inhibitors, gonadotropin releasing hormone stimulant, urofollitropins, muscle relaxants such as neuromuscular blocking agents, prostaglandin analogs, prostaglandins, prostaglandin inhibitors, respiratory therapy agents, anticholinergics, beta adrenergic stimulators, sympathomimetics, and thrombolytics, antithrombotics, anticoagulants, antibiotics antiplatelet agents, thrombolytics, antiproliferatives, steroidal and nonsteroidal antiinflammatories, agents that inhibit hyperplasia and in particular restenosis, smooth muscle cell inhibitors, growth factors, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters and drugs that may enhance the formation of healthy neointimal tissue, including endothelial cell regeneration agents, clonidine, estradiol, nicotine, nitroglycerin, and scopolamine steroidal and nonsteroidal antiinflammatory drugs, antibacterials, antiprotozoals, antifungals (e.g., nystatin); coronary vasodilators (e.g., nitroglycerin); calcium channel blockers (e.g., nifedipine, diltiazem); bronchodilators (e.g., theophylline, pirbuterol, salmeterol, isoproterenol); enzyme inhibitors such as collagenase inhibitors, protease inhibitors, elastase inhibitors, lipoxxygenase inhibitors and angiotensin converting enzyme inhibitors (e.g., captopril, lisinopril); other antihypertensives (e.g., propranolol); leukotriene antagonists (e.g., ICI 204,219); anti-ulceratives such as H<sub>2</sub> antagonists; steroidal hormones (e.g., progesterone, testosterone, estradiol, levonorgestrel); antivirals and/or immunomodulators (e.g., 1-isobutyl-1H-imidazo[4,5-c]quinolin-4-amine, 1-(2-hydroxy-2-methylpropyl)-1H-imidazo[4,5-c]quinoline-4-amine, and other compounds disclosed in U.S. Pat. No. 4,689,338, incorporated herein by reference, acyclovir); local

anesthetics (e.g., benzocaine, propofol); cardiotonics (e.g., digitalis, digoxin); antitussives (e.g., codeine, dextromethorphan); antihistamines (e.g., diphenhydramine, chlorpheniramine, terfenadine); narcotic analgesics (e.g., morphine, fentanyl); peptide hormones (e.g., human or animal growth hormones, LHRH); cardioactive products such as atriopeptides; proteinaceous products (e.g., insulin); enzymes (e.g., anti-plaque enzymes, lysozyme, dextranase); antinauseants (e.g., scopolomine); anticonvulsants (e.g., carbamazine); immunosuppressives (e.g., cyclosporine); psychotherapeutics (e.g., diazepam); sedatives (e.g., phenobarbital); hypnotics; anticoagulants (e.g., heparin); analgesics (e.g., acetaminophen); antimigraine agents (e.g., ergotamine, melatonin, sumatriptan); antiarrhythmic agents (e.g., flecainide); antiemetics (e.g., metaclopramide, ondansetron); anticancer agents (e.g., methotrexate); neurologic agents such as anxiolytic drugs; hemostatics; anti-obesity agents; antigout agents; antianxiety agents; antiinflammatory agents; hormones; immunosuppressive agents; hypolipedemic agents; antiparkinson agents; antifungal agents; analgesics; antimanic agents; antipyretics; antiarthritic agents; antiplatelet agents; anticonvulsants; antidiabetic agents, anticoagulants, antiarrhythmics, antianginal agents; and the like, as well as pharmaceutically acceptable salts, esters, solvates and clathrates thereof.

8. The composition according to claim 1 wherein said lipidized polymer is a lipidized protein.

9. The composition according to claim 8 wherein said protein is selected from the group consisting of enzymes, cell surface proteins, hormones, antibodies, growth factors, clotting factors, neuroproteins, tumor suppressors, toxins, antigens and epitopes of antigens, apolipoproteins, endogenous or exogenous tumor antigenic proteins, bioinvasive molecules (like bacterial invasins), lectins, lectin-like molecules, bacterial toxins such as cholera and macromolecules with bioadhesive properties.

10. The composition according to claim 8 wherein said protein is selected from immunoglobulins, epitopes, transferrin, avidin, hormones, enzymes, integrin, apolipoprotein E, apolipoprotein B100, and mixtures, thereof.

11. The composition according to claim 8 wherein said protein is lysozyme, avidin, apolipoprotein B100 or apolipoprotein E.

12. The composition according to claim 1 wherein said lipid core comprises a mono-, di- or triglyceride.

5 13. The composition according to claim 10 wherein said lipid core comprises triglycerides.

14. The composition according to claim 10 or 11 wherein said mono-, di- or triglyceride is obtained by esterifying glycerol with a fatty acid selected from the group consisting of palmitic, stearic, oleic, linoleic, linolenic and mixtures, thereof.

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15. The composition according to claim 12 wherein said triglyceride is triolein.

16. The composition according to claim 1 wherein said triglycerides are vegetable oils selected from the group consisting of linseed oil, iticica oil, tung oil, soybean oil, sunflower oil, safflower oil, palm oil, poppy seed oil, corn oil, sesame seed oil, olive oil, canola oil, cottonseed oil, castor oil, coconut oil and mixtures, thereof.

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17. The composition according to claim 1 wherein said bioactive agent is boronated cholesterol.

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18. A method of enhancing the bioavailability of a bioactive agent in a patient comprising administering to said patient a composition comprising:

i. a microemulsion comprising a lipid core and an amphipathic lipid layer surrounding said lipid core, wherein a hydrophobic portion of said amphipathic lipid layer is associated with said lipid core and a hydrophilic portion of said amphipathic lipid layer is associated with a hydrophilic surface of said amphipathic lipid;

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ii. a bioactive agent; and

iii. optionally, a lipidized polymer;

said bioactive agent being included in said composition in an effective amount, said amphipathic lipid being included in said composition in an amount effective to form a microemulsion with said lipid core, and said lipidized polymer being included in said composition in association with said amphipathic lipid in an amount ranging from about 0.01% to about 65% by weight of said composition.

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19. The method according to claim 18 wherein said lipidized polymer is a lipidized targeting protein and said bioavailability of said bioactive agent is enhanced in one or more tissues of said patient.

20. The method according to claim 19 wherein said targeting protein is selected from the group consisting of immunoglobulins, immunogens, transferrin, avidin, lysozyme, hormones, enzymes, integrin, monoclonal antibodies and mixtures, thereof.

21. The method according to claim 18 wherein said lipidized polymer is lysozyme, avidin or polylysine.

22. A method of enhancing the bioavailability of a bioactive agent to a predetermined site or tissue within a patient comprising administering to said patient a composition comprising:

i. a microemulsion comprising a lipid core and an amphipathic lipid layer surrounding said lipid core, wherein a hydrophobic portion of said amphipathic lipid layer is associated with said lipid core and a hydrophilic portion of said amphipathic lipid layer is associated with a hydrophilic surface of said amphipathic lipid;

ii. a bioactive agent; and

iii. a lipidized polymer;

said bioactive agent being included in said composition in an effective amount, said amphipathic lipid being included in said composition in an amount effective to form a microemulsion with said lipid core, and said lipidized polymer is a lipidized targeting protein included in said composition in association with said amphipathic lipid in an amount ranging from about 0.01% to about 65% by weight of said composition.

23. The method according to claim 18 wherein said lipidized targeting protein is selected from the group consisting of immunoglobulins, immunogens, transferrin, avidin, lysozyme, hormones, enzymes, integrin, monoclonal antibodies and mixtures, thereof.

24. The method according to claim 19 wherein said targeting protein is lysozyme or avidin.

25. A method of enhancing the stability of a microemulsion, said microemulsion comprising a lipid core and an amphipathic lipid layer surrounding said lipid core, wherein a hydrophobic portion of said amphipathic lipid layer is associated with said lipid core and a

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32. The method according to claim 28 wherein said bioactive agent is BCH.

Parameter	Value	Unit
Temperature	25.0	°C
Pressure	1.0	atm
Flow rate	1.0	L/min
Concentration	0.1	mol/L
pH	7.0	
Wavelength	254	nm
Scan rate	1.0	nm/min
Integration time	1.0	s
Resolution	0.5	nm
Slit width	1.0	mm
Detector	Photodiode array	
Software	ChemStation	
Column	C18	
Mobile phase	Water/Acetonitrile	
Gradient	0-100% ACN in 10 min	
Flow rate	1.0	mL/min
Injection volume	10	μL
Sample concentration	1.0	mg/mL
Calibration	Linear	
Correlation coefficient	0.999	
Limit of detection	0.1	μg/mL
Limit of quantification	0.3	μg/mL
Recovery	100	%
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	% RSD
Precision	1.0	% RSD
Accuracy	1.0	% RSD
Robustness	1.0	% RSD
Linearity	1.0	% RSD
Specificity	1.0	% RSD
Sensitivity	1.0	% RSD
Reproducibility	1.0	% RSD
Stability	1.0	%

33. A pharmaceutical composition comprising:

i. a microemulsion comprising a lipid core and an amphipathic lipid layer surrounding said lipid core, wherein a hydrophobic portion of said amphipathic lipid layer is associated with said lipid core and a hydrophilic portion of said amphipathic lipid layer is associated with a hydrophilic surface of said amphipathic lipid;

ii. an effective amount of a bioactive agent selected from the group consisting of cholesterol 1,12-dicarba-closo-dodecaborane 1-carboxylate, cholesterol 1,2-dicarba-closo-dodecaborane 1-carboxylate, cholesterol 1,7-dicarba-closo-dodecaborane 1-carboxylate and mixtures, thereof; and

ii. optionally, a lipidized polymer;

said bioactive agent being included in said composition in an effective amount, said amphipathic lipid being included in said composition in an amount effective to form a microemulsion with said lipid core, and said lipidized polymer being included in said composition in association with said amphipathic lipid in an amount ranging from about 0.01% to about 65% by weight of said composition.

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